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REMARKS

Claims 1-8 are pending. Claim 6 has been withdrawn as being drawn to a non-elected invention. Claims 1-8 are cancelled herein. New claims 9-14 are presented herein. Accordingly, new claims 9-14 are under consideration.

Support for new claims 9-14 is found throughout the specification and in the original claims. Specifically, support for new claims 9-13 is found, for example, in original claims 1-5, respectively. Support for new claim 14 is found, for example, in original claim 8. No issue of new matter is introduced by this amendment.

Applicants note that the Examiner mentioned several references in the Office Action, including: Great Britain Patent No. 2,283,239; United States Patent No. 6,6117,312, which number includes a typographical error, and has, therefore, been understood to refer to United States Patent No. 6,617,312; and PCT Application Nos. WO 97/44451 and WO 99/27104, as being of interest. Applicants agree with the Examiner that none of these references is deemed relevant to the method of the present invention.

Priority

The Examiner has acknowledged applicants' claim for foreign priority under 35 U.S.C. 119 (a-d) and has accorded to the present application the priority date of August 24, 2000. Applicants respectfully submit that now cancelled claims 1-8 and newly presented claims 9-14 are entitled to a priority date of September 1, 1999, based on an application filed in the United Kingdom (GB Application No. 9920673.2) to which the present application claims priority. The Examiner is referred to the Request for Filing a Continuation or Divisional Application of an International Application (submitted March 1, 2002) and the executed Declaration and Power of Attorney for Patent Application (submitted May 24, 2002) for confirmation. Applicants respectfully request that the record of the present invention be rectified to reflect the correct priority date of September 1, 1999.

Specification

The specification is objected to as failing to provide proper reference to the drawings. The Examiner states that the specification refers to Figs. 1, 2, 3a-3c, and 4a-4c, but alleges that the application contains only Figures 3a, 3c, and 4b. Applicants respectfully submit that the application does include Figs. 1, 2, 3a-3c, and 4a-4c, which drawings were filed with the application and explicitly acknowledged by the United States Patent and Trademark Office by return postcard. Applicants submit that the objection to the specification is, therefore, improper. Accordingly, applicants respectfully request that the objections to the specification be withdrawn.

Rejections 35 USC § 112

Claims 1-5 and 7-8 have been rejected under 35 U.S.C. §112, first paragraph, on the basis as understood, that the claimed invention purportedly lacks sufficient enablement. Claims 1-8 are cancelled herein, thereby obviating the rejection of these claims. Applicants address the rejection, however, as it may be applied to newly presented claims 9-14. The Examiner acknowledges that the specification is enabling for a method for treating allergic rhinitis. The Examiner, however, appears to contend that the experimental evidence presented in the specification is allegedly not sufficient to demonstrate that non-infective or allergic rhinitis can be prevented with the claimed histacalin proteins. Applicants strenuously disagree with the Examiner with regard to this rejection. In view of the experimental evidence presented in the specification, which clearly demonstrates a preventative effect of histacalin protein (EV 504/VAC life) pre-treatment for allergic rhinitis induced by histamine, and applicants' arguments hereinbelow, applicants assert that new claims 9-14 are fully enabled by the specification.

To begin, it should be noted that the Examiner refers to the challenge of subjects with EV 504 or VAC life. Applicants respectfully assert that this statement is incorrect. The specification clearly teaches that EV 504/VAC life is another designation for the histamine binding protein MS-HBP1 of the invention. See page 9, lines 18 to 20. As such, administration of EV 504 or VAC life to the subjects does not constitute "challenging" the subjects. On the

contrary, EV 504/VAC life serves a therapeutic/preventive role, whilst histamine is used to challenge the subjects and induce allergic rhinitis. See page 9, line 4.

As shown in an Example of the specification, the effect of EV 504/VAC life administration on subjects was investigated. See page 9. Briefly, a pre-treatment histamine challenge was administered to subjects whose nasal secretions and airway resistance were measured 45 minutes later. The subjects were then treated with EV 504/VAC life and then 15 minutes later the subjects were administered a post-treatment histamine challenge, after which nasal secretions and airway resistance were once again measured. The nasal secretion and airway resistance measurements for pre- and post-EV 504 treatment are shown in Figures 1 to 4c. As can be clearly seen from Figures 3a to 4c, the "Pre VAC life" readout (i.e. nasal secretion and nasal airway resistance prior to the administration of EV 504/ VAC life) is considerably higher than the "Post VAC life" readout. This clearly shows that EV 504/VAC life is capable of preventing allergic rhinitis because, despite the administration of histamine 15 minutes subsequent to the administration of EV 504/VAC life, nasal secretions and airway resistance are considerably reduced in subjects treated with EV 504/VAC life as compared to those of subjects to whom only histamine is administered (Pre VAC life measurements).

Claims 1-5 and 7-8 have been further rejected under 35 U.S.C. §112, first paragraph, for an alleged lack of enablement based on recitation of the terms "functional equivalent" or an "active fragment" of a histacalin of the invention. Specifically, the Examiner has contended that *"in the absence of demonstrated evidence of record that said pharmaceutical composition comprising "functional equivalent" or an "active fragment" of histacalin protein, or MS-HBP1, FS-HBP1, FS-HBP2 or D.RET6 protein would treat allergic rhinitis upon administering of said composition to a patient in need thereof, the claimed invention is not considered enabled."* Claims 1-8 are cancelled herein, thereby obviating the rejection of these claims. Applicants will, however, address the rejection so as to render apparent that a similar rejection, should it be applied to newly presented claims 9-14, would be unfounded.

The term "functional equivalent" is defined on page 4, lines 1 to 5 as a protein which *"contains single or multiple amino-acid substitution(s), addition(s), insertion(s) and/or deletion(s) from the wild type protein sequence and/or substitutions of chemically-modified amino acids that do not affect the biological function of binding to its respective vasoactive amine"* (emphasis added)

The term "active fragment" is defined on page 4, lines 6 to 8 as a *"truncated protein that retains the biological function of binding to its respective vasoactive amine"* (emphasis added).

Because the terms "functional equivalent" and "active fragment" are by definition (see underlined language above) proteins which retain the biological activity of the wild type protein, it follows that "functional equivalents" and "active fragments" employed in the present invention are useful in treating allergic rhinitis. If, for example, a fragment of the histacalin protein does not retain the vasoactive amine binding properties of the histacalin protein, then the fragment does not fall within the definition of "active fragment" as used in the present application.

It is common general knowledge that protein sequences may be modified to give rise to similar sequences having comparable properties. Moreover, many methods for generating such protein sequences are available and well known in the art. Such methods are readily applied to the generation of fragments or functional equivalents of the histacalin proteins of the invention. An appreciation that various modifications may be made to the histacalin proteins, MS-HBP1, FS-HBP1, FS-HBP2 and D.RET6 without compromising the biological activity of the proteins is underscored by the sequence comparison shown in Table 1 of the specification. Despite the limited number of conserved residues, all of the proteins shown in Table 1 are capable of binding to vasoactive amines, demonstrating that related proteins within this family are capable of treating and preventing allergic rhinitis. Notably, although few in number, the conserved residues are features of the histacalin protein family that contribute to functionality. Table 1, therefore, presents considerable guidance with which an ordinarily skilled practitioner can design and generate fragments or functional equivalents of the histacalin proteins of the invention.

Moreover, it is the Examiner's position that the specification teaches "*administration of a pharmaceutical composition comprising only a few concentrations of only the histacalin protein*". Applicants direct the Examiner's attention to page 8, lines 1-20, wherein various routes for administration of the histacalin proteins of the invention are described and ranges of effective doses indicated. As presented in the specified passages, an effective dose is between 0.01 μg/kg and 50 μg/kg, with a more particular range of between 0.05 μg/kg and 10 μg/kg. For intranasal administration, for example, an effective dose of a histacalin protein in solution is 0.1 μg/ml and 100 μg/ml. An effective dose of a histacalin protein in solution for intranasal delivery is further defined as between 0.1 μg/ml and 10 μg/ml, and more particularly elaborated between 1 μg/ml and 8 μg/ml. See page 8, lines 15-20. In view of the above, applicants submit that the specification provides ample guidance pertaining to effective dosage of a histacalin protein of the invention. Applicants, therefore, assert that the Examiner's comments directed to alleged deficiencies pertaining to effective doses of a histacalin protein are without basis.

In view of the above arguments and the support found in the specification for the subject matter as originally claimed, applicants contend that the rejection of now cancelled claims 1-8 under 35 U.S.C. §112, first paragraph, was improper. It is submitted that should such a rejection be considered as applicable to presently submitted claims 9-14, it would be equally unfounded.

Claims 2-3, 5, and 7-8 have been rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Claims 1-8 have been cancelled, thereby mooting the rejection of these claims under 35 U.S.C. §112, second paragraph.

Accordingly, the Examiner is respectfully requested to consider the new claims in light of evidence found in the specification and arguments presented herein above.

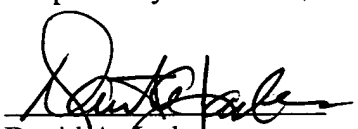
Fees

No additional fees are believed to be necessitated by this amendment. However, should this be an error, authorization is hereby given to charge Deposit Account No. 11-1153 for any underpayment or to credit any overpayment.

Conclusion

It is submitted, therefore, that the claims are in condition for allowance. No new matter has been introduced. From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order, and such action is earnestly solicited. In the event that there are any questions concerning this amendment, or application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of this application may be expedited.

Respectfully submitted,



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